

U.S.S.N. 08/700,565  
GRUENBERG  
AMENDMENT

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JUL 17 2000

TECH CENTER 1600/2000

~~214. The method of claim 1, wherein density of the cells is at least  $10^9$  cells/liter. —~~

~~— 215. The method of claim 1, wherein density of the cells is at least  $10^{10}$  cells/liter. —~~

~~— 216. The method of claim 22, wherein density of the cells is at least  $10^9$  cells/liter. —~~

~~— 217. The method of claim 22, wherein density of the cells is at least  $10^{10}$  cells/liter. —~~

Please cancel claims 2, 3, 5, 7, 14, 16, 17, 154 without prejudice or disclaimer.

Please amend claims 1, 8, 22 and 155 as follows:

1. (Amended) A method for selectively stimulating proliferation and differentiation of T lymphoid cells to generate [generating] a high density of clinically relevant numbers of T lymphoid cells, comprising:

collecting material comprising body fluid or tissue containing mononuclear cells from a mammal;

treating the cells are under conditions whereby *ex vivo* differentiation of the cells into Th1, Th1-like, Th2-like or Th2 cells is induced; and

contacting, in the absence of exogenous interleukin-2, the material with two or more activating proteins specific for cell surface proteins present on cells in the material and in an amount sufficient to induce *ex vivo* cell expansion, whereby the cells expand to [clinically relevant numbers at a density of] at least about [ $10^9$ ]  $10^{10}$  cells regulatory cells of one predominant phenotype [ in a volume of about a liter].

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8. (Amended) The method of claim 1, wherein the expanded cells are predominantly Th1 or Th2[ or Th3] cells.

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22. (Twice Amended) A method for generating clinically relevant cell numbers of regulatory T lymphoid cells, comprising:

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- (a) collecting material containing mononuclear T lymphoid cells from a mammal;
  - (b) activating the T lymphoid cells to alter their cytokine production profile by causing differentiation of the cells to regulatory cells; and
  - (c) inducing cell proliferation and expanding the cells under conditions that produce [high cell density of] at least about 10<sup>10</sup> cells/liter [10<sup>9</sup> cells/liter and produce clinically relevant number] of a homogeneous population of regulatory T lymphoid cells.

155. (Amended) A method for generating clinically relevant numbers of regulatory T lymphoid cells for autologous cell therapy, comprising:

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- (a) collecting material comprising body fluid or tissue containing mononuclear cells from a mammal;
  - (b) treating the cells to induce differentiation of mononuclear cells into regulatory T cells, wherein regulatory T cells are mononuclear cell that have the ability to control or direct an immune response, but do not act directly as effector cells in the response; and
  - (c) contacting the resulting differentiated cells with [one] two or more activating proteins specific for cell surface proteins present on the cells in an amount sufficient to induce *ex vivo* cell expansion, whereby clinically relevant numbers of regulatory cells for autologous cell therapy are generated.

REMARKS

A check for the fee for a three month extension of time accompanies this response. Any fee that may be due in connection with this application may be